Acceleration of fetal maturation by intra-amniotic administration of thyroxine

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Spontaneously occurring Hyperthyroidism of the fetus secondary to transplacentally acquired LATS, has been known to accelerate markedly fetal maturation, including that of the skeletal system.

The purpose of this study was to examine the effectiveness of induced fetal hyperthyroidism upon the rate of fetal maturation among patients who were likely to go into pre-term labor, or in whom pre-term delivery hat been planned either for maternal or fetal indications.

The present report summarizes our experience of the initial 15 patients (Fig.1). Indications for thyroxine therapy. Maternal indications were: severe heart disease, pulmonary fibrosis (HERMANSKI-PUDLAK Syndrome), leukemia, cancer of cervix, CNS A-V malformation, and placenta previa. Fetal indications included, hemolytic anemia due to Rh-antibodies, MECKELS syndrome (renal and CNS malformation) of one of the twins, triplet gestation, and pre-term rupture of membranes. Evaluation of mother and fetus prior to the administration of thyroxine. The assessment consisted of documentation of fetal age by history and sonographic measurements of the fetus, maternal T_3, T_4 and TSH, frequency of fetal heart rate and fetal movements (as detected by mother), and composition of amniotic fluid (L/S, Creatinine and Bilirubin).

AGE, BIRTH WEIGHT AND APGAR SCORE OF 15 PRE-TERM NEWBORNS DELIVERED AFTER PRENATAL TREATMENT OF INTRA-AMNIOTIC THYROXINE

	MEAN	RANGE
AGE (WEEKS)	33.3	29.6 - 35.3
BIRTH WEIGHT (GRAMS)	2,156	1,560 - 2,930
APGAR SCORE AT 5 MINUTES	8.5	7-9

Thyroxine was injected into the amniotic space in doses ranging from 200 to 500 mg and was repeated either weekly or in a 3 day interval.

The indicators used to assess the impact of thyroxine therapy upon mother and fetus were identical with those used for initial assessment, except for signs and symptoms suggestive of maternal hyperthyroidism (eq. palpitations, anxiety and insomnia).

Only 3 of the 15 mothers displayed signs of mild and transient hyperthyroidism which was observable 48 hours after the administration of the second dose and disappeared within 2 days.

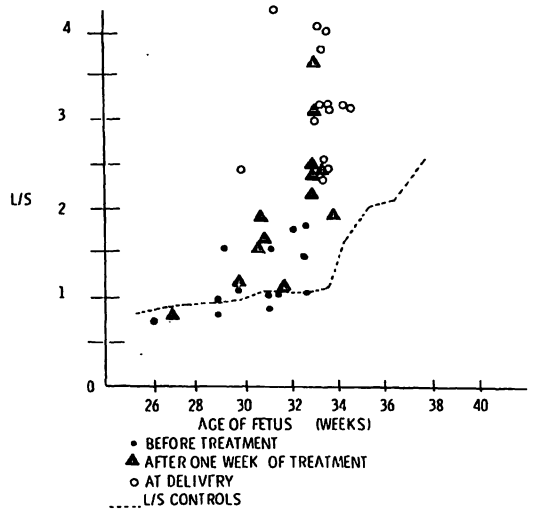
There was an increase of fetal movement (both frequency and intensity) all instances, which increase was

noted first after 48 hours of the initial dose of thyroxine.

Heart rate of the fetus increased only moderately ranging from 5 to 20 beats per minute.

The pre-treatment L/S had a mean value of 1.16 and the mean of the gestational age was 30.6 weeks (Fig.2 and 3). Although the mean duration of therapy to reach

L/S RATIO OF AMNIOTIC FLUID OF FETUSSES TREATED WITH INTRA-AMNIOTIC INJECTION OF THYROXINE



AGE OF FETUS, INITIAL L/S, AND DURATION OF INTRA-AMNIOTIC THYROXINE THERAPY (TO THE TIME WHEN THE L/S WAS ≥ 2 OF 15 PATIENTS

	MEAN	RANGE
AGE (WEEKS)	30.6	26.0 - 33.2
INITIAL L/S	1.16	0.70 - 1.75
DURATION OF THERAPY TO L/S 2* (DAYS)	11.4 DAYS	3.0 - 27.0

*EARLIEST L/S OF 2 AT 29.6 WEEKS

an L/S 2 was 11.4 days, the median was only 7 days. In 2 patients a change of L/S from 1.43 and 1.75 to 2.35 and 2.60 respectively occurred in less than 4 days.

P.G.Values were obtained on only one patient, in whom it changed from undetectable to 3.3 over a period of one week.

It is evident that L/S of the treated population differ markedly from those derived from a large control group (dotted line).

Although in one case L/S of 2.4 was observed at 29.6 weeks of gestation following 4 weeks of thyroxine therapy, in all others the principal change occurred between the 31 and 33 weeks. The lesser responsiveness of the younger fetuses might be explained on the basis of their limited capacity to transform the adminstered T_4 into T_3.

Effect on growth and general maturation of the fetus was assessed by comparing birth weight and DUBOWITZ scores against respective standards at matched gestational age. Reference standard for expected birth weight was 50 percentile of the LUBCHENKO nomogram.

The mean birth weight was 258 grams above that predicted from the nomogram, and the mean of the DUBOWITZ score was 2.26 weeks ahead of the chronologic age of the fetus.

Bone age was determined only on one infant; it was 3

weeks above the chronologic age. Neonatal complications consisted of mild RDS in 1 of 16 newborns, transient tachypnea in 3, and in-utero acquired pneumonia in 2. Only two of the newborns required assisted ventilation. All newborns were enrolled in a special surveillance program under the direction of a pediatric endocrinologist.

Follow-up to date has failed to disclose any unusual clinical problems. Only one of the 16 newborns received thyroxine postnatally for reasons unrelated to clinically detectable Hypothyroidism. None had suppressed TSH levels, or abnormal T_3 or T_4 concentrations. The triplets exhibited an above average growth pattern for the first two months, and received blood transfusion for anemia.

Our inital experience supports the view that a relatively mild degree of fetal hyperthyroidism brought about by intraamniotic administration of thyroxine, accelerates fetal maturation, while at the same time increasing fetal growth. Thyroxine appears to be superior to glucocorticoids to prevent sequelae of immaturity.

It is probable that T_3 is even more efficatious to achieve this objective than T_4, due to the limited capacity of the younger fetus to transform T_4 into T_3.

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